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Chronic kidney failure often progresses from early **stage** (partial) to **end stage** (complete) failure. There is **no cure** for **end-stage renal** failure (ESRF) also known as **end-stage renal disease** (ESRD). The damage done to the kidneys is irreversible. Treatment at the **end stage** of kidney failure involves replacing the lost functions of your kidneys by dialysis or by a kidney transplant.

There are two kinds of dialysis treatment, hemodialysis and peritoneal dialysis. Dialysis patients:

- manage their fluid balance by adjusting what they drink
- manage the substances such as calcium and other nutrients that their bodies have to deal with by watching their **renal** diet
- are tested to monitor the effectiveness of their dialysis

Transplantation is another treatment option. You will learn about the tests used for determining if a patient is suitable for receiving a transplant, and for monitoring a transplant.

Dialysis patients are monitored and/or treated by the medical team in a Dialysis center.

Convenient summaries are provided of:

HIGHLIGHTED CONTENT

If you have not enrolled in Stay In Touch don't wait another day! This education program for kidney patients and their families can be delivered right in your email inbox.

Need help telling family, friends and employers?

Positive things you can do to adjust to a new way of life

Learn more about the types of dialysis treatments

- Hemodialysis
- Peritoneal dialysis

What you should know about kidney transplants

What you should know if you choose none of the treatment options

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End stage kidney failure

If you have been recently diagnosed with kidney failure, this section will help you understand your situation:

- What to expect next;
- What happens at a Dialysis center (where you will have your future appointments);
- All about the different tests you might be given.

As well as discussing the practical aspects of your care, we take a look at how you may be feeling in initial reactions, and discuss some different approaches which may help you come to terms with your diagnosis and how it makes you feel. You may be dreading telling people about your illness - our sections on telling family and friends and on telling employers will help you prepare for these important discussions.

The treatments available for kidney failure have advanced dramatically over the last 10 years. While there is still **no absolute cure**, the quality of life and flexibility of lifestyle patients can look forward to now far exceeds what was possible a generation ago. The treatment of kidney failure section looks at the different types of dialysis and transplant available to replace the function of your kidneys. We also look at the treatments you may be prescribed that deal with some of the side-effects of kidney failure - anemia, high blood pressure and **renal bone disease**.

If you have recently been diagnosed with kidney failure, it is normal to feel shocked and overwhelmed by what is happening to you and what lies ahead. At this **stage** you may have a period of years before your kidney function becomes inadequate, or you may need dialysis in the near future.

You may not have noticed the symptoms of your illness because they may have developed very gradually. Once patients start treatment, however, most of them realize how poorly they had been feeling, because of the noticeable improvements once treatment starts.

Dialysis and transplant patients can find practical tips on dealing with daily life, travel, and exercise in the Coping and living section of the site.

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Characterization of peptidyl boronic acid inhibitors of mammalian 20 S and 26 S proteasomes and their inhibition of proteasomes in cultured cells

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Abbreviations used: Boc, N-t-butoxycarbonyl; Bz, benzoyl; Cbz, benzyloxycarbonyl; AMC, 7-amido-4-methylcoumarin; NAP, β-naphthylamide; suc, succinyl; TNF-α, tumour necrosis factor-α.

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Key words: chymotrypsin-like activity, tight binding inhibitors, NF-κB.

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Proteasomes are large multisubunit proteinases which have several distinct catalytic sites. In this study a series of di- and tri-peptidyl boronic acids have been tested on the chymotrypsin-like activity of purified mammalian 20 S and 26 S proteasomes assayed with succinyl-Leu-Leu-Val-Tyr-amidomethylcoumarin (suc-Leu-Leu-Val-Tyr-AMC) as substrate. The inhibition of 20 S proteasomes is competitive but only slowly reversible. The K_i values for the best inhibitors were in the range 10–100 nM with suc-Leu-Leu-Val-Tyr-AMC as substrate, but the compounds tested were much less effective on other proteasome activities measured with other substrates. Free boronic acid inhibitors exhibited equivalent potency to their pinacol esters. Both benzoyl (Bz)-Phe-boroLeu and benzyloxycarbonyl (Cbz)-Leu-Leu-boroLeu pinacol ester inhibited 20 S and 26 S proteasomes with non-ideal behaviour, differences in inhibition of the two forms of proteasomes becoming apparent at high inhibitor concentrations (above $3 \times K_i$). Both of these compounds were also potent inhibitors of 20 S and 26 S proteasomes in cultured cells. However, gel filtration of cell extracts prepared from cells treated with radiolabelled phenacetin-Leu-Leu-boroLeu showed that only 20 S proteasomes were strongly labelled, demonstrating differences in the characteristics of inhibition of 20 S and 26 S proteasomes. The usefulness of peptidyl boronic acid inhibitors for investigations of proteasome-

mediated protein degradation was confirmed by the observation that Bz-Phe-boroLeu and Cbz-Leu-Leu-boroLeu pinacol ester inhibited NF κ B activation with IC₅₀ values comparable to their K_i values for purified proteasomes. The latter result supports the view that the chymotrypsin-like activity of proteasomes assayed with suc-Leu-Leu-Val-Tyr-AMC is a critical one for protein degradation in cells.

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Degradation pathways of a peptide boronic acid derivative, 2-Pyz-(CO)-Phe-Leu-B(OH)(2).

Wu S, Waugh W, Stella VJ.

Department of Pharmaceutical Chemistry, the University of Kansas, 2095 Constant Avenue, Lawrence, Kansas 66047, USA.

The peptide boronic acid derivative 2-Pyz-(CO)-Phe-Leu-B(OH)(2) is a potent inhibitor of 20S proteasome and a proposed anticancer agent. During preformulation studies, the compound presented erratic stability behavior. Efforts were made to isolate and identify the degradation products, thereby helping to identify possible mechanisms for the degradation. The reaction of 2-Pyz-(CO)-Phe-Leu-B(OH)(2) with hydrogen peroxide not only provided a convenient way to isolate the initial degradation products seen from hydrolysis in aqueous buffers but also showed that the major, initial degradation pathway was probably oxidative in nature. The isolated degradation products were characterized by nuclear magnetic resonance spectroscopy, mass spectrometry, and optical rotation dispersion. In the presence of hydrogen peroxide, the boronic acid group was cleaved from 2-Pyz-(CO)-Phe-Leu-B(OH)(2) to give an alcohol with an apparent retention of the original stereochemistry. Subsequent isomerization and further hydrolysis were then seen. Surprisingly, added ascorbate and EDTA accelerated rather than inhibited degradation. Degradation of 2-Pyz-(CO)-Phe-Leu-B(OH)(2) under acidic and basic conditions seemed to be mediated by an initial oxidative degradation pathway similar to that seen with the peroxide. Copyright 2000 Wiley-Liss, Inc. and the American Pharmaceutical Association J Pharm Sci 89: 758-765, 2000.

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